this Amendment, claims 3-5 and 11-14 will be pending and under examination.

Pursuant to the requirements of 37 C.F.R. §1.121, applicants annex hereto as **Exhibit A**, a marked-up version of the amended claim.

Rejection under 35 U.S.C. §112, Second Paragraph

The Examiner rejected claim 6 under 35 U.S.C. §112, second paragraph, as allegedly indefinite. Specifically, the Examiner asserted that claim 6 depends on cancelled claim 1 or 2.

In response to the Examiner's rejection, but without conceding the correctness thereof, applicants note that claim 6 has been cancelled.

Rejection under 35 U.S.C. §112, First Paragraph

The Examiner rejected claims 3-6 and 11-14 under 35 U.S.C. §112, first paragraph, as allegedly not providing an adequate written description of a method for preventing exaggerated restenosis in a diabetic subject which comprises administering to the subject a pharmaceutically effective amount of an inhibitor of receptor for advanced glycation endproducts (RAGE) so as to prevent exaggerated restenosis in the subject.

Specifically, the Examiner asserted that the disclosure in the specification is not sufficient to convey to one skilled in the art that applicants were in possession of numerous polypeptide inhibitors of RAGE for the claimed method in the present invention.

Further, the Examiner asserted that the specification only discloses using sRAGE for the claimed method.

In response to the rejection of claim 6, applicants point out that this claim has been cancelled, rendering the rejection thereof moot.

In response to the Examiner's rejection of claims 3-5 and 11-14, applicants respectfully traverse. Applicants point out that amended claims 3-5 and 11-14 do not recite "polypeptide inhibitors of RAGE" but rather "sRAGE."

In view of the above remarks, applicants maintain that claims 3-5 and 11-14 satisfy the requirements of 35 U.S.C. §112, first paragraph.

Further, the Examiner rejected claims 3-6, 9, and 11-14 under 35 U.S.C. §112, first paragraph, as allegedly not enabled.

In response to the rejection of claims 6 and 9, applicants point out that these claims have been canceled, making the rejection thereof moot.

Applicants respectfully traverse the Examiner's rejection with regard to claims 3-5 and 11-14. Amended claims 3-5 and 11-14 provide a method for preventing exaggerated restenosis in a diabetic subject which comprises administering to the subject a therapeutically effective amount of sRAGE so as to prevent exaggerated restenosis in the subject.

The test for enablement under 35 U.S.C. §112, first paragraph, is whether the disclosure contains sufficient information regarding the subject matter of the claims to enable one skilled in the relevant art to practice the claimed invention without undue experimentation.

The Examiner concedes that the specification is enabling for reduction of smooth muscle proliferation and migration in carotid artery by treating Fatty Zucker rat with sRAGE via intraperitoneal injection. However, the Examiner asserts that the specification does not provide adequate guidance and evidence that any inhibitor of RAGE, including sRAGE, can prevent exaggerated restenosis in a diabetic subject.

In response, applicants respectfully point out that this assertion of a lack of enablement is contrary to the Examiner's own comments in the April 10, 2002 Office Action. There, the Examiner conceded that the specification *is* enabling for preventing exaggerated restenosis in a diabetic subject by administering to said subject sRAGE.

Specifically on page 6, the Examiner stated that the "specification fails to provide adequate guidance and evidence for how to inhibit new tissue growth or neointimal formation in blood vessels in a subject or preventing exaggerated restenosis in a diabetic subject by administering to said subject ... any polypeptide inhibitor of RAGE other than sRAGE *in vivo*." (emphasis added).

On page 7, the Examiner stated that "[i]n view of the lack of detailed information regarding the structural and functional

requirements of the polypeptide inhibitor of RAGE, and the unpredictability of polypeptide function from mere amino acid sequence, it would be unpredictable [whether] any polypeptide other than sRAGE or polypeptide having a molecular weight of about 500 daltons to about 100 kilodaltons would function as inhibitor of RAGE to inhibit new tissue growth or neointimal formation in blood vessels in a subject or preventing exaggerated restenosis in a diabetic subject *in vivo*." (emphasis added).

Further, applicants are not aware of any requirement under 35 U.S.C. §112, first paragraph, that mandates providing human experimental data in order to enable claims supported by data from an animal model, provided that the animal model adequately represents a human subject with respect to the disease in question. Applicants maintain that the disclosed rats, which suffer from type 2 diabetes, are an adequate representation of humans suffering from diabetes. The Zucker fatty rat was studied because it is a model of insulin resistance, hyperglycemia, hyperlipidemia and obesity. This model, in certain respects, at least, typifies the characteristics of human subjects with type 2 diabetes. Applicants maintain that the data presented in the specification using this model would be expected to correlate with human results. The Examiner has not cited any art which indicates otherwise.

Applicants therefore maintain that additional (e.g. human) data are not required and that the experimental data disclosed in the subject application are sufficient to enable the pending claims. Indeed, section 2164.02 of the M.P.E.P. states that an "in vitro or in vivo animal model example in the specification, in effect, constitutes a 'working example' if that example 'correlates' with a

disclosed or claimed method invention." The Examiner concedes that the instant claims are enabling for the reduction of smooth muscle proliferation and migration in carotid artery by treating Fatty Zucker rat with soluble RAGE (sRAGE) via intraperitoneal injection. Applicants assert that at the very least, these methods and their results in mice would be expected to "correlate" with such methods and their results in humans. The Examiner has failed to set forth art indicating a lack of correlation between the animal model example disclosed in the specification and the claimed methods for treating subjects including humans.

Accordingly, applicants maintain that claims 3-5 and 11-14 satisfy the requirements of 35 U.S.C. §112, first paragraph.

Further, the Examiner rejected claim 9 under 35 U.S.C. §112, first paragraph, as allegedly containing new matter. Specifically, the Examiner asserted that the phrase "V-domain of soluble receptor for advanced glycation endproduct (sRAGE)" is considered new matter.

In response to the Examiner's rejection, but without conceding the correctness thereof, applicants point out that claim 9 has been canceled, thereby rendering the rejection moot.

Sequence Listing

The Examiner asserted that this application fails to comply with the requirements of 37 C.F.R. §§1.821-1.825 as set forth in the Notice to Comply with Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures, attached as **Exhibit B**. Specifically, the Notice

asserts that the application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. §1.821(c) and a copy of the "Sequence Listing" in computer readable form as required by 37 C.F.R. §1.821(e).

In response, applicants annex hereto a paper copy of the Sequence Listing as **Exhibit C**, enclose a C.R.F. of the corrected Sequence Listing, and annex hereto a Statement in Accordance with 37 C.F.R. §1.821(f) as **Exhibit D**.

Summary

For the reasons set forth hereinabove, applicants maintain that the claims pending are in condition for allowance, and respectfully request allowance.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

No fee, other than the $55.00 fee for a one-month extension of time, is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.

4/21/03

Alan J. Morrison
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